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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BARTON, JEFFREY THOMAS	
ART UNIT	**PAPER NUMBER**
1753	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/052,601	ROBERT, FREDERIC	
	Examiner	Art Unit	
	Jeffrey T. Barton	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-25 and 30-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 8-25, and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 23 April 2007 has been entered.

Status of Objections and Rejections Pending Since the Office Action of 15 June 2006

2. The objections to claims 1 and 30-32 are withdrawn due to Applicant's amendment.

3. The rejection of claim 31 under 35 U.S.C. §112, second paragraph is withdrawn due to Applicant's amendment.

4. The rejection of claims 12-14 and 30 under 35 U.S.C. §103(a) as unpatentable over Keo et al, Lehninger, Lau, and Swank et al is withdrawn.

5. The rejection of claims 12-15 and 30 under 35 U.S.C. §103(a) as unpatentable over Keo et al, Lehninger, Lau, and Lehninger is withdrawn.

6. All other rejections are maintained.

Claim Objections

7. Applicant is advised that should claim 12 be found allowable, claim 30 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 3, 8-11, 16-19, 21-25, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al (U.S. Patent 5,599,433) in view of Lehninger, Principles of Biochemistry, pp. 706-707, (1982) and Lau (U.S. Patent 5,194,390).

Keo et al teaches the capillary zone electrophoresis (CZE) of glycosylated proteins in clinical specimens from humans, wherein the buffer system contains, for example, 100 mM CAPS (which reads on the instant biological buffer), 300 mM sodium borate (which reads on the instant additive that increases ionic strength), and NaOH for adjusting the pH to 11 (see col. 1, lines 19-23; col. 3, lines 32-55; col. 4, lines 43-49; col. 5, line 16 through col. 6, line 14; and col. 8, lines 32-43). The sodium borate concentration can be 50 to 200 mM (see col. 5, lines 43-65). The clinical specimen can be a human biological liquid such as serum, plasma, cerebrospinal fluid, urine, etc (see col. 6, lines 17-22). With respect to claims 18 and 19, said CAPS is a C_9 alkylsulfonate. With respect to claim 21, and as noted above, the CAPS has a concentration of 100

mM. Thus, for example, 1 mm or 5 mM of the 100 mM CAPS corresponds to the 1 to 5 mM alkylsulfonate in claim 21, while the remaining 99 mM or 95 mM CAPS corresponds to the instant buffer. Keo et al teaches the limitations of the instant claims other than the differences which are discussed below.

Keo et al does not specifically require that said buffer system containing, for example, 100 mM CAPS, 300 mM sodium borate, and NaOH be used for the serum, plasma, cerebrospinal fluid, or urine biological fluid. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used said buffer system containing 100 mM CAPS, 300 mM sodium borate, and NaOH for the serum, plasma, cerebrospinal fluid, or urine biological fluid because such is clearly within the scope of Keo et al's disclosure.

With respect to claim 1 and its dependent claims, Keo et al does not specifically teach that its clinical sample contains the instant protein constituent. As noted above, Keo et al teaches that its clinical sample can be human plasma or urine. Lehninger is relied upon for showing that over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Lau is relied upon for teaching what is well known, i.e., that approximately one third of total urinary protein is serum albumin (see col. 1, lines 52-57). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used plasma or urine as Keo et al's clinical sample because such is clearly within the scope of Keo et al's disclosure. Over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in

Table 24-3 at page 707 of Lehninger, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Furthermore, approximately one third of total urinary protein is serum albumin, as shown by Lau.

With respect to claim 32, it is noted that this claim recites that "said buffer system does not contain borate". However, Keo et al does not require that its complexing agent be borate (see abstract; col. 3, lines 25-55; and claim 1 at cols. 9-10). Indeed, Keo et al's claim 1 recites a complexing agent, but does not recite or require borate. Borate is an example, of Keo et al's complexing agent. It would have been well within the skill of an artisan to have used a suitable complexing agent, other than borate, for Keo et al's complexing agent because such is clearly within the scope of Keo et al's disclosure.

12. Claims 2 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al in view of Lehninger and Lau as applied to claims 1, 3, 8-11, 16-19, 21-25, and 32 above, and further in view of Krylov et al, "Capillary Electrophoresis for the Analysis of Biopolymers," Anal. Chem., pages 111R-128R (2000).

Keo et al in view of Lehninger and Lau is relied upon for the reasons recited above. With respect to claims 2 and 31, Keo et al teaches that that, using the CZE, the glycoproteins are separated from any other proteins in the sample (see col. 3, lines 59-62). As noted above, albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins are in plasma, and serum albumin is in urine. Accordingly, using the CZE, said albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins are separated from the glycoproteins when the sample is plasma, and serum albumin is separated from the glycoproteins

when the sample is urine. Thus, the requirement in instant claims 2 and 31 of "separating" is achieved when Keo et al performs the CZE on the plasma or urine. With respect to the requirement of "detecting said protein constituents" in claim 2, Keo et al teaches that the electrophoretically separated proteins are detected by a suitable method, such as measurement of light absorption at 415 nm. The detection of proteins is conventional in the art. Indeed, Krylov et al teaches that UV absorption can be used to detect proteins, and, in Table 1 at the bottom of page 116R shows that UV absorbance has been used to detect human plasma proteins when separated by CZE (see also the Detection section at pages 118R-124R). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have detected the plasma proteins after Keo et al's separation because detection of proteins is well known in the art, and, indeed, Krylov et al teaches that UV absorption can be used to detect proteins and shows that UV absorbance has been used to detect human plasma proteins when separated by CZE. With respect to claim 31, when the proteins are detected, they are also analyzed.

13. Claims 12-14 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al, Lehninger, and Lau as applied to claims 1, 3, 8-11, 16-19, 21-25, and 32 above, and further in view of Chen. (J. Chromatogr. Reference)

Keo et al, Lehninger, and Lau teach a method as described above in addressing claims 1, 3, 8-11, 16-19, 21-25, and 32.

None among Keo et al, Lehninger, and Lau explicitly teach providing an additive that increases ionic strength selected from among the listed alkali metal salts.

Chen teaches a method for free-zone capillary electrophoretic separation of serum proteins, and teaches that increasing the ionic strength of the borate buffer by adding salt increases the resolution attained in the separation. (Results and Discussion section; 1st 3 paragraphs)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the buffer of Keo et al by adding salt to increase the ionic strength, as taught by Chen, because Chen teaches that this increases the resolution of serum proteins in free-zone capillary electrophoretic separations. In the absence of further description, one having ordinary skill in the art would have understood the term "salt" to mean sodium chloride.

14. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al, Lehninger, Lau, and Chen as applied to claims 12-14 and 30 above, and further in view of Ohmura et al. (US 5,521,287)

Keo et al, Lehninger, Lau, and Chen teach a method as described above in addressing claims 12-14 and 30.

None among these references explicitly teach increasing the ionic strength of the buffer using sodium sulfate as an additive.

Ohmura et al teaches that salts for adjusting ionic strength include KCl and sodium sulfate (see the paragraph bridging Columns 7 and 8).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Keo et al, Lehninger, Lau, and Chen by substituting the salt used in the buffer with sodium sulfate, because the substitution of art recognized equivalent salts for adjusting ionic strength, as shown by Ohmura et al, would have been within the skill of an artisan. The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945).

15. Claims 1, 3, 8-14, 16-25, 30, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al in (U.S. Patent 5,599,433) view of Lehninger, Principles of Biochemistry, pp. 706-707, (1982), Lau (U.S. Patent 5,194,390), and Jones et al (U.S. Patent 5,366,601).

Keo et al teaches the capillary zone electrophoresis (CZE) of glycosylated proteins in clinical specimens from humans, wherein the buffer system contains, for example, 100 mM CAPS (which reads on the instant biological buffer), 300 mM sodium borate (which reads on the instant additive that increases ionic strength), and NaOH for adjusting the pH to 11 (see col. 1, lines 19-23; col. 3, lines 32-55; col. 4, lines 43-49; col. 5, line 16 through col. 6, line 14; and col. 8, lines 32-43). The sodium borate concentration can be 50 to 200 mM (see col. 5, lines 43-65). The clinical specimen can be a human biological liquid such as serum, plasma, cerebrospinal fluid, urine, etc (see col. 6, lines 17-22). With respect to claims 18 and 19, said CAPS is a C_9 alkylsulfonate.

With respect to claim 21, and as noted above, the CAPS has a concentration of 100 mM. Thus, for example, 1 mm or 5 mM of the 100 mM CAPS corresponds to the 1 to 5 mM alkylsulfonate in claim 21, while the remaining 99 mM or 95 mM CAPS corresponds to the instant buffer. Keo et al teaches the limitations of the instant claims other than the differences which are discussed below.

Keo et al does not specifically require that said buffer system containing, for example, 100 mM CAPS, 300 mM sodium borate, and NaOH be used for the serum, plasma, cerebrospinal fluid, or urine biological fluid. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used said buffer system containing 100 mM CAPS, 300 mM sodium borate, and NaOH for the serum, plasma, cerebrospinal fluid, or urine biological fluid because such is clearly within the scope of Keo et al's disclosure.

With respect to claim 1 and its dependent claims, Keo et al does not specifically teach that its clinical sample contains the instant protein constituent. As noted above, Keo et al teaches that its clinical sample can be human plasma or urine. Lehninger is relied upon for showing that over 70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Lau is relied upon for teaching what is well known, i.e., that approximately one third of total urinary protein is serum albumin (see col. 1, lines 52-57). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used plasma or urine as Keo et al's clinical sample because such is clearly within the scope of Keo et al's disclosure. Over

70% of the plasma solids in blood plasma is attributed by the plasma proteins listed in Table 24-3 at page 707 of Lehninger, and include the instant albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins. Furthermore, approximately one third of total urinary protein is serum albumin, as shown by Lau.

With respect to claims 12-14 and 20, Keo et al does not specifically teach that its buffer contains an additive such as sodium octanesulfonate (see col. 7, lines 15-35). Jones et al teaches the capillary zone electrophoresis of anionic species, wherein sodium octanesulfonate is used in the buffer as an electromigration agent. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have added the sodium octanesulfonate to Keo et al's capillary zone electrophoresis buffer so as to take advantage of the sodium octanesulfonate's known function in capillary zone electrophoresis, i.e., as an electromigration aid, as taught by Jones et al.

16. Claims 2 and 31 rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al in view of Lehninger, Lau, and Jones et al as applied to claims 1, 3, 8-14, 16-25, 30, and 32 above, and further in view of Krylov et al, "Capillary Electrophoresis for the Analysis of Biopolymers," Anal. Chem., pages 111R-128R (2000).

Keo et al in view of Lehninger and Lau is relied upon for the reasons recited above. With respect to claims 2 and 31, Keo et al teaches that that, using the CZE, the glycoproteins are separated from any other proteins in the sample (see col. 3, lines 59-62). As noted above, albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins are in plasma, and serum albumin is in urine. Accordingly, using the CZE, said albumin, α_1-

globulin, α_2-globulin, β-globulins, and γ-globulins are separated from the glycoproteins when the sample is plasma, and serum albumin is separated from the glycoproteins when the sample is urine. Thus, the requirement in instant claims 2 and 31 of "separating" the protein constituents is achieved when Keo et al performs the CZE on the plasma or urine. With respect to the requirement of "detecting said protein constituents" in claim 2, Keo et al teaches that the electrophoretically separated proteins are detected by a suitable method, such as measurement of light absorption at 415 nm. The detection of proteins is conventional in the art. Indeed, Krylov et al teaches that UV absorption can be used to detect proteins, and, in Table 1 at the bottom of page 116R shows that UV absorbance has been used to detect human plasma proteins when separated by CZE (see also the Detection section at pages 118R-124R). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have detected the plasma proteins after Keo et al's separation because detection of proteins is well known in the art, and, indeed, Krylov et al teaches that UV absorption can be used to detect proteins and shows that UV absorbance has been used to detect human plasma proteins when separated by CZE. With respect to claim 31, when the proteins are detected they are also analyzed.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-3, 8-25, and 30-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 5, 7-25, 27-30, and 33-36 of copending Application No. 10/052,931. Although the conflicting claims are not identical, they are not patentably distinct from each other because in claim 23 of said copending application, the buffer can be a zwitterionic biological buffer. As seen in the specification of said copending application the "zwitterionic biological buffer" encompasses buffers such as CAPS.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

19. Applicant's arguments filed 23 April 2007 have been fully considered but they are not persuasive.

Applicant argues that it would not have been obvious to use the method of Keo et al for analysis of the claimed proteins. This is not persuasive because Keo et al unambiguously suggest that the samples to be separated can be plasma or urine (Column 6, lines 18-22) Lehninger and Lau show that the claimed proteins are contained in these materials. Since there is thus no distinction between the instant samples and those taught by Keo et al, the limitations of the claim are clearly met. Whether or not Keo et al is concerned with specifically tailoring the method for analysis of the claimed sample constituents is irrelevant. The method involves performing electrophoresis on a sample containing the claimed proteins using a buffer as claimed, and all steps of the method are taught by the prior art.

Applicant argues that it would not have been obvious to use a buffer containing a sugar complexing agent other than borate within the method of Keo et al, because a skilled artisan would have recognized that borate forms stable complexes with and imparts a negative charge to the hemoglobin. This does not exclude selection of other complexing agents. Keo et al does not require that its complexing agent be borate (see abstract; col. 3, lines 25-55; and claim 1 at cols. 9-10). Indeed, Keo et al's claim 1 recites a complexing agent, but does not recite or require borate. Borate is an example of Keo et al's complexing agent. It would have been well within the skill of an artisan to have used a suitable complexing agent, other than borate, for Keo et al's complexing agent because such is clearly within the scope of Keo et al's disclosure.

Applicant argues that the preamble of instant claim 1 does not merely state a desired effect, but recites an intentional purpose. This does not change the fact that

each method step is taught or suggested by the prior art, as put forth in the rejection above, which clearly renders the claim obvious. The samples suggested by Keo et al contains the instantly claimed proteins, as shown by Lehninger and Lau, and the limitations of the method steps are therefore met.

Applicant's arguments against the combination of Keo et al with Lehninger are irrelevant, because Lehninger's pages 706-707 are relied upon simply to show what is well known, that plasma contains the instantly claimed proteins. The teaching of analysis of this sample is within Keo et al, as clearly stated in the rejection. Applicant's arguments are entirely irrelevant to the rejection.

In response to Applicant's argument that Keo et al do not teach or suggest separation of the instant sample constituents, the Examiner responds that Keo et al clearly teach that the Hb A1c is separated from other protein constituents. (Column 3, lines 59-62) Although the focus of Keo et al is on determination of Hb A1c, this separation meets the instant separation limitation, because the instantly claimed proteins, which are present in the sample of Keo et al must be separated from the Hb A1c.

Applicant somehow attempts to argue that a skilled artisan would not use the method of Keo et al to analyze plasma or urine. (Paragraph bridging pages 15 and 16 of the Remarks). In response, the Examiner cites column 6, lines 18-22 of Keo et al again, which clearly suggests that plasma and urine samples are to be injected into the capillary for electrophoresis.

Applicant's arguments against the rejections based on the teachings of Krylov et al are not persuasive, because Krylov teaches that UV absorption can be used to detect proteins and shows that UV absorbance has been used to detect human plasma proteins when separated by CZE. Detection of proteins in the sample other than glycosylated hemoglobin would have been obvious also because it is suggested by Keo et al. (Column 7, lines 1-9) Krylov et al is a review article of capillary electrophoresis for the analysis and separation of biopolymers. A skilled artisan would use Keo et al's buffer for Keo et al's procedure, and would follow the capillary zone electrophoresis procedures in Krylov et al's Table 1 at page 116R when those procedures are performed. The issue here is what is well known and conventional in the art with respect to the detection of proteins. Krylov et al has been relied upon for showing what is very well known and conventional in the art, i.e., that detection of proteins is conventional. Indeed, Krylov et al teaches that UV absorption can be used to detect proteins, and, in Table 1 at the bottom of page 116R shows that UV absorbance has been used to detect human plasma proteins when separated by CZE (see also the Detection section at pages 118R-124R). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have detected the plasma proteins after Keo et al's separation because detection of proteins is well known in the art, and, indeed, Krylov et al teaches that UV absorption can be used to detect proteins and shows that UV absorbance has been used to detect human plasma proteins when separated by CZE.

Applicant argues that Jones et al does not disclose that octanesulfonate can be used in a process other than with ionic molecules. However, this argument is not deemed to be persuasive because proteins are ionic in solution.

Applicant argues that there is no suggestion that octanesulfonate can be used as an additive in a migration system to improve the separation of proteins. However, this argument is not deemed to be persuasive because the only positively recited step in each of independent claims 1, 30, and 32 is the step of "introducing" the clinical sample into the capillary column, which is precisely what Keo et al does. Claim 31 recites "analyzing or separating serum protein constituents selected albumin, a_1-globulin, a_2-globulin, β-globulin, β_1-globulin, β_2-globulin and γ-globulin". However, the term "separating" is so broad that is can be interpreted to mean what Keo et al is doing, i.e., separating the albumin, α_1-globulin, α_2-globulin, β-globulins, and γ-globulins that are in the plasma from the glycoproteins so that the glycoproteins can be analyzed. The Examiner maintains that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have added the sodium octanesulfonate to Keo et al's capillary zone electrophoresis buffer so as to take advantage of the sodium octanesulfonate's known function in capillary zone electrophoresis, i.e., as an electromigration aid, as taught by Jones et al.

Applicant argues that the Examiner has not read the references as a whole, but is merely relying on narrow teachings with the present invention in mind. Such general allegations hardly overcome the motivations clearly provided in the rejections, and explained repeatedly in the Office Actions. In response to applicant's argument that the

examiner is using improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey T. Barton whose telephone number is (571) 272-1307. The examiner can normally be reached on M-F 9:00AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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